istence of these particular hydrophobic bonds is manifested in deoxygenated, concentrated hemolysates by reversible sol-gel transformations at 0° and 37°C. Deoxygenated hemolysates of S hemoglobin gel at 37°C and liquefy at 0°C. In such systems, demonstration of reversible, temperature-dependent sol-gel transformations (a negative temperature coefficient of gelation is specific for S hemoglobin or the S structural variant, hemoglobin C (Harlem). The test is simple, has clear end-points, will detect both homozygous and heterozygous S hemoglobin, and is specific.

The molecular mechanism for sickling of hemoglobin S has been so precisely defined by the Murayama hypothesis that by extension we have selected on theoretical grounds urea as a chemical desickling agent. Urea attacks intertetrameric hydrophobic bonds implicated by Murayama to break those specific pathogenetic bonds formed in part by the substituted valine residues. Urea forms new hydrophobic bonds of its own with the improperly structured hemoglobin S tetramer, altering the steric structure of the hemoglobin S molecule WITHOUT adversely affecting the vital function of oxygen transport. Thus, by chemical manipulation, a lethal molecular property is inhibited by steric hindrance with the formation of urea-hemoglobin complex, since tetrameric polymerization or "stacking," that is, sickling, is impossible.

PAUL L. WOLF, M.D.

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Value of Histochemistry in the Investigation of Human Muscle Diseases

Awareness of the value of histochemical techniques in the investigation of human neuromuscular disorders has increased in the last few years. Such studies have allowed the definition of two or more fiber types, recognition of abnormalities in the reactivity and localization of biochemically defined organelles, determination of the magnitude of collateral reinnervation from type-specific fiber grouping and precise identification of regenerative activity and inflammation.

With such procedures, significant advances have been made in our understanding of the identification and pathogenesis of unusual muscle disorders including nemaline, central core, myotubular and vacuolar myopathy. Increased use of morphometric analysis of fiber types has proved of prognostic and therapeutic value. Newer approaches have placed emphasis on the recognition of the differential susceptibility of fiber types to degeneration or atrophy in a variety of neurogenic and myopathic disorders. Further advances in the recognition and investigation of myopathies will require the continued association of clinician and pathologist.

M. ANTHONY VERITY, M.D.

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Prenatal Diagnosis of Inherited Diseases

A specimen of amniotic fluid (about 10 ml) taken between the 14th and 16th week of pregnancy contains viable cells of fetal origin. The sex of the fetus, chromosomal abnormalities and certain enzyme defects can be diagnosed from these cells after two to four weeks in cell culture. The combined maternal and fetal risk of amniocentesis (probably less than 1 percent) is substantially less than the risk of giving birth to an affected child in families at risk for a detectable genetic disorder (25 percent) or in pregnancies occurring in women over 40 years of age (3 percent). The procedure is not universally applicable, however; not all genetic diseases, and none of the dominant or polygenically inherited disorders, can be detected. The